REMARKS

Claims 1, 2, 4-7 and 9-19 presently appear in this case. No claims have been allowed. Claims 6, 11, 14, 15 and 19 have been withdrawn from consideration. The official action of June 20, 2006, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention relates to a method of detecting a proliferative-related disease state that is a tumor or psoriasis in a subject, or for determining the severity of such a disease state, or for determining whether a patient having such a disease state has a high probability of responding to a therapeutic treatment involving the administration of an A3AR agonist or antagonist. Cells suspected of being in the disease state are tested to detect the level of expression of A3AR in control cells indicative of a normal state. This difference in levels is indicative of the disease state and is correlated to the severity of disease state, and is further indicative that the subject has a high probability of responding to a therapeutic treatment by an A3AR agonist or antagonist.

The examiner has agreed that claims 1, 2, 7, 16 and 17 are linking claims that link all the claims of groups I-VI together and that, upon the allowance of a linking claim, the restriction requirement as to the linked invention will be withdrawn and any claims depending from or otherwise including all the limitations of the allowable linking claim will be entitled to examination in the instant application. As it is

believed that the present response establishes that the linking claims are allowable, prompt consideration and allowance of all the claims now present in the case are respectfully urged.

The examiner states that the first line of the specification should be updated if applicant desires priority under 35 U.S.C. §119(e) based on a previously filed application. The examiner makes reference to the O.G. notice at 1268 OG 89 (18March2003) for additional information. This requirement is respectfully traversed.

The examiner's attention is respectfully invited to 37 C.F.R. §1.78(a)(2)(iii), which states:

> If the later-filed application is a non-provisional application, the reference required by this paragraph must be included in an application data sheet (§1.76), or the specification must contain or be amended to contain such reference in the first sentence(s) following the title.

As the examiner referred to the O.G. Notice 1268 OG 89, the examiner's attention is invited to Part IV thereof, which states:

> The reference required by 37 C.F.R. § 1.78(a)(2) or (a)(5) must be included in an application data sheet (37 C.F.R. 1.76) or the specification must contain, or be amended to contain, such reference in the first sentence following the title.

See also the first sentence of Part V, which is to the same effect.

An application data sheet was filed with the present application on filing. Accordingly, there is no requirement to insert reference to the prior filed provisional application

in the first line of the specification. However, upon review of this ADS, it has been noted that an error was made therein, in that it specifies that the present application is a division of application number 60/420,038, rather than that this application claims priority under 35 U.S.C. §119(e) of provisional application 60/420,038. Accordingly, a substitute application data sheet is filed herewith to correct this error. Reconsideration and withdrawal of this rejection to the specification are respectfully urged.

Claims 3 and 8 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite for reciting the term "a proliferative-related disease state" and "proliferative disease state." The examiner states that the meaning of these terms is unclear. The examiner recognizes that the instant specification defines proliferative disease as cancer or other proliferative disease such as psoriasis at page 9, lines 4-5. However, the specification does not teach the "other proliferative disease" and the language reads on any diseases that cause a cancer or are resulting from a cancer. This rejection is respectfully traversed.

All of the claims have now been amended to specify that the method relates to "a proliferative-related disease state that is a tumor or psoriasis." This language is no longer indefinite, to the extent that it ever was. It does not read on diseases that cause a tumor or cause psoriasis. It specifies that the disease state is a tumor or psoriasis. This is now sufficiently definite to comply with the second

paragraph of 35 U.S.C. §112. Reconsideration and withdrawal of this rejection is respectfully urged.

Claims 1-3, 7, 8, 12, 13, 16 and 17 have been rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for a method of detecting a tumor in a subject, a method for detecting the severity of a tumor in a subject and a method for determining whether a subject has a high probability of responding to a therapeutic treatment of a tumor comprising detecting the level of expression of A3AR in the tumor cells, does not reasonably provide enablement for a method of detecting any and all disease states in a subject. The examiner is clearly objecting to the claims because of the breadth of the term "disease state". This rejection is respectfully traversed.

All of the claims are now directed to detecting a proliferative-related disease state that is a tumor or psoriasis. The examiner concedes that the present specification is enabling for the methods relating to tumors. However, now the only other embodiment falling within the "proliferative-related disease state" language is psoriasis, which as the examiner recognizes is specifically mentioned in the present specification. As the specification is enabled for tumors, there is no reason to believe that the present invention would not also be operable for psoriasis. Accordingly, in view of the amendment to the claims, reconsideration and withdrawal of this rejection is respectfully urged.

Claims 1-5, 7-10, 12, 13 and 16-18 have been rejected under 35 U.S.C. §102(a) as being anticipated by Madi in view of the teaching of Wei. and Keyomarsi. The examiner states that Madi teaches detection of A3AR protein in melanoma and colon carcinoma cells and shows that A3AR is highly expressed in these tumor cells. The examiner believes that the teachings of Wei and Keyomarsi fill the deficiencies of Madi with respect to Madi's lack of a teaching comparing the level of A3AR protein expressed in melanoma and colon carcinoma cells with a control level or to the values of a predetermined calibration curve. This rejection is respectfully traversed.

Attached hereto is a declaration of under 37 C.F.R. §1.132 signed by Dr. Pnina Fishman, one of the present inventors, which declaration establishes that the relevant part of the disclosure of the Madi reference is the conception of the present inventors and therefore, cannot be considered to be a prior publication of "another" as required by 35 U.S.C. § 102(a). As stated in the declaration, the concept that tumor cells have high expression of A3AR is that of Lea Madi, Sara Ben-Yehuda and Pnina Fishman, jointly, without inventive input from any of the other three co-authors of the paper. The declaration specifies that while all six were properly named as authors, as all contributed to the experimentation reported in the abstract, the three authors who are not inventors were technicians or students who assisted the inventors, but did not contribute to this

conception. All worked directly or indirectly at the direction of Dr. Fishman, and/or under the direction of Lea Madi and Sara Ben-Yehuda, so as to prove the conception of the present of the inventors about abnormally high expression of this receptor, but they did not contribute to the original concept. Accordingly, analogous to the situation *In re Katz*, 687 F.2d 450, 215 USPQ 14(CCPA 1982), and as authorized in the MPEP, for example at MPEP 715.01(c)I, this declaration should be sufficient to remove the publication as a reference under 35 U.S.C. §102(a). Note the above-cited section of the MPEP where it states:

> [T]he Applicant may overcome the rejection by filing a specific affidavit or declaration under 37 C.F.R. § 1.132 establishing that the article is describing applicant's own work. An affidavit or declaration by applicant alone indicating that applicant is the sole inventor and that the others were merely working under his or her direction is sufficient to remove the publication as a reference under 35 U.S.C. §102(a).

As Madi is not a statutory bar under 35 U.S.C. §102(b) and is not the work of "another", so that 35 U.S.C. §102(a) is not available, this publication has been removed as a reference against the present application. As the rejection requires the Madi reference, elimination of Madi as a reference, eliminates the rejection. Reconsideration and withdrawal of this rejection is therefore respectfully urged.

Claims 1-5, 7-10, 12, 13 and 16-18 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Baraldi in view of the teaching of Reeves, Wei and Keyomarsi.

The examiner states that Baraldi teaches a method for determining tumor cells which possess a high concentration of adenosine A3 receptors in a patient or in a cell sample by administering to the patient or to the sample a radiolabeled compound which can be detected following binding of the compound to tumor cells, allowing the compound to bind to tumor cells and detecting the radiolabel when the compound selectively binds A3AR. The examiner recognizes that Baraldi does not teach detecting adenosine A3 receptor protein or mRNA, nor comparing the level of the expression of A3AR to a control level or to the values of a calibration curve, nor does Baraldi teach correlating the level of the expression of A3AR with the severity of the tumor. However, the examiner considers that these deficiencies are made up for in the teaching of Reeves, Wei and Keyomarsi. This rejection is respectfully traversed.

Baraldi discloses compounds endowed with selective A3 adenosine receptor agonist activity, and suggests that the compounds may be used in the detection and/or treatment of cancer (column 14, lines 31-34). Baraldi further states that tumor cells have been shown to express the A3 receptor (column 14, lines 32-34; column 15, lines 8-16), and shows the characterization of A3 receptors in some human tumor cell lines (example 18, column 39). However, the A3 receptor appears on many types of cells and fulfills a variety of functions, as taught by Baraldi (column 1, lines 37-50). Nowhere does Baraldi teach the expression of A3AR in normal

cells nor the differential expression of A3AR on cancerous as compared to normal cells. Therefore, Baraldi does not teach a method for determining the presence of tumor cells among normal cells, but rather a method for determining the presence of the A3 receptor on cells, which are already known to be tumor cells.

The present application on the other hand, provides examples demonstrating A3AR protein expression in a number of tumor cell types as compared to normal cells. These include colon carcinoma cells (examples 1-4), breast cancer cells (examples 2, 3, 4) and melanoma cells (example 5). This is not at all taught by Baraldi.

Reeves does not cure the deficiencies of Baraldi as Reeves merely discloses A3 anti-peptide anti-sera. Wei suggests a diagnostic assay for detecting altered levels of hdCK2 protein in various tissues as compared to normal control tissue samples to detect the presence of a disease and Keyomarsi discloses correlation of cycline E protein aberration to different stages of breast cancer. However, neither Wei nor Keyomarsi teach anything about the use of A3AR to detect tumor cells in a subject. Accordingly, no combination of Baraldi, Reeves, Wei and Keyomarsi make obvious the processes of the present invention. Reconsideration and withdrawal of this rejection are therefore respectfully urged.

Claims 1, 2, 7, 12, 13, 16 and 17 have been provisionally rejected on the ground of non-statutory obvious-type double patenting as being unpatentable over claims 1, 2,

5 and 15 of co-pending application 10/565,238. This rejection is respectfully traversed.

It is noted that the present rejection was not applicable to claims 3 or 8. All of the present claims are now specifically directed to detecting or determining the severity of or the probability of response to treatment for proliferative-related disease states. As application 10/565,238 relates only to inflammation and as the examiner has already agreed that those claims directed to proliferative-related disease states are not subject to this rejection, reconsideration and withdrawal of this double patenting rejection are respectfully urged.

It is submitted that all the claims now present in the case clearly define over the references of record. Reconsideration and allowance are therefore earnestly solicited.

Respectfully submitted,

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